

AREA OF EMPHASIS:

Training, Infrastructure, and Capacity Building

SCIENTIFIC ISSUES

In the United States, African American and Latino/Hispanic adolescents bear the largest proportion of newly diagnosed HIV infections, and African American women of all ages, and the elderly of all races, are disproportionably affected by HIV/AIDS. Not enough minority-focused efforts have been implemented to interrupt this trend. It is urgent to develop scientifically sound and culturally and ethnically sensitive programs to encourage African and Hispanic Americans' active participation in these efforts, from the conception to the development and implementation of HIV prevention interventions and research.

There is a need for more minority health care professionals, including but not limited to scientists, physicians, counselors, and nurses. Initiatives to create a pool of well-trained biomedical and behavioral minority HIV/AIDS investigators as well as individuals trained in technical support areas should start at the high school level by encouraging students to consider careers in science. In addition, new training and mentoring mechanisms should be created to attract recent graduates to the HIV/AIDS research field. Similar programs must be implemented to draw established scientists from related fields. Basically, current and better training mechanisms should be encouraged to improve the recruitment and retention of minority scholars. Mentoring opportunities are essential for the success of these training programs.

The new international initiatives for the provision of antiretroviral therapies to many undeveloped countries have emphasized the need for training of medical and scientific in-country leadership to participate in setting the research agenda.

In-country training programs for biomedical and behavioral personnel to meet the immediate needs of therapeutic and prevention clinical trials in resource-poor countries greatly affected by the HIV/AIDS epidemic are also needed. Expansion of these programs must include training in ethics issues (providing materials in the native language especially for the establishment of ethics boards), clinical trials, behavioral and social sciences, technology transfer, and informatics. These training programs should be culturally adapted to the region.

In addition to well-trained personnel, appropriate infrastructure must be in place to conduct HIV-related research both in the United States and in foreign research institutions. The indispensable infrastructure for supporting such research includes well-equipped laboratories, computer and data management capabilities, inpatient and outpatient space for clinical research, and associated health and laboratory personnel. Research management support must also be in place to ensure responsible stewardship of funds. Mechanisms are also needed for long-term infrastructure maintenance in resource-poor countries.

HIV/AIDS biomedical prevention testing (e.g., vaccines and microbicides) depends mainly on the use of nonhuman primate (NHP) models. Expanded animal facilities are still needed, not only to house experimentally infected NHP (biosafety level [BSL]-2/-3 facilities) but also to breed the appropriate number of specific pathogen-free (SPF) animals required for HIV/AIDS research.

TRAINING PROGRAMS

Although NIH-funded programs have expanded the number of U.S. training positions in AIDS-related research, an increased focus on African American and Latino trainees is still needed. The predoctoral and postdoctoral training supported by the NIH from non-AIDS funds that provides broad interdisciplinary training and prepares investigators to undertake AIDS-related research must also be tailored to fulfill the needs of the highly affected minority population.

The NIH Loan Repayment Program (LRP) was mandated by Congress under Public Law 100-607 in 1988, authorized under 42 USC 288-1, and reauthorized under Public Law 103-43 to encourage health professionals to engage in AIDS-related research at the NIH. Since FY 1989, 148 professionals (through FY 2003/4) have been attracted to the NIH intramural research program. Based on voluntary disclosure, only 11 percent of participants were African Americans and 7 percent Latinos. This program should be expanded to create a center of attention for qualified African American, American Indian, and Latino graduates to participate in HIV/AIDS research at the NIH laboratories.

The John E. Fogarty International Center (FIC) sponsors several programs focused on strengthening the international research capacity in developing countries and emerging democracies. The AIDS International Training and Research Program

(AITRP) and the International Clinical, Operational, and Health Services Research and Training Award for AIDS and Tuberculosis (ICOHRTA AIDS/TB) program provide research training related to HIV. AITRP is a multidisciplinary program designed to promote research capacity in the epidemiology, prevention, diagnosis, treatment, and care of HIV/AIDS in developing countries and emerging democracies; to facilitate the evaluation of AIDS drugs and vaccines internationally; and to provide global scientific leadership in HIV/AIDS. This program is cofunded by seven other NIH Institutes and Offices (ICs). ICOHRTA AIDS/TB cooperative agreements are awarded to institutions in developing countries and emerging democracies with strong HIV/TB-related research experience and to the U.S. and developed-country institutions with which they have established HIV/TB collaborations. Seven other NIH ICs, the Centers for Disease Control and Prevention (CDC), and the U.S. Agency for International Development (USAID) cofund this program.

The FIC Global Health Research Initiative Program (GRIP) is intended to promote productive reentry of NIH-trained foreign investigators into their home countries as part of a broader program to enhance the scientific research infrastructure in developing countries, and to stimulate research on HIV/AIDS health-related issues in these countries. GRIP provides partial salaries to foreign researchers returning home, as well as support for their research projects. Eleven other NIH ICs support this program.

The FIC Global Infectious Disease Research Training Program (GID) provides research training in other infectious diseases, including TB and HIV-related coinfections. The FIC research training programs have facilitated the conduct of many international research studies supported by other NIH ICs in a wide range of research disciplines, particularly in resource-poor settings. However, more programs need to be developed and supported to build research capacity to deter the AIDS epidemic in the world.

The National Cancer Institute (NCI) has addressed, domestically, the training need for clinicians and clinical researchers to study AIDS-related malignancies. This training should be focused to increase the number of participating minority institutions and investigators.

The National Institute of Mental Health (NIMH) and the National Institute of Child Health and Human Development (NICHD), through the Center for AIDS Prevention Studies (CAPS) in San Francisco, support two model training programs that seek to enhance research capacity in both domestic minority populations and international trainees. The first is a minority investigators training program that provides mentoring and technical assistance to minority visiting professors who plan to conduct research on HIV risk behavior in minority populations. The second is an international scholars program, which provides research training for international

scientists and builds partnerships to promote productive international research with these scholars. These programs should be duplicated by other ICs to stimulate not only behavioral modification and prevention studies but also basic and clinical research projects.

In different regions of the world, a driving force of the AIDS epidemic is the injecting drug users (IDUs) who share dirty needles or equipment. The National Institute on Drug Abuse (NIDA) offers training opportunities that provide research skills necessary for addressing the joint epidemics of drug abuse and HIV/AIDS. These include the INVEST Drug Abuse Research Fellowship Program that can be used to train foreign fellows in AIDS research in U.S. laboratories and NIDA's Distinguished International Scientist Award Program, which supports exchange visits and promotes collaborations between U.S. and international scientists interested in drug abuse and HIV/AIDS-related research. To curtail the HIV epidemic, stronger and sustained efforts are needed to train more scientists within affected communities in these specific areas.

NIH ICs need to expand and retain the cadre of new investigators in critically needed research areas, such as social and behavioral sciences. The Behavioral Science Track Award for Rapid Transition (B/START) program, sponsored by NIMH and NIDA, is designed specifically to assist new behavioral scientists in entering the behavioral research environment through expedited application and review procedures. These programs have to emphasize HIV/AIDS research to allow new investigators to conduct HIV/AIDS studies.

The National Institute of Allergy and Infectious Diseases (NIAID) has developed the Comprehensive International Program of Research on AIDS (CIPRA) to provide infrastructure and capacity building to institutions from developing countries. Through this mechanism, the host country institutions participate in the preparation for large-scale HIV vaccine trials and prevention clinical trials, and they also have the capacity to perform volunteer counseling and testing in their local populations, both to identify new HIV infections and to perform in-country the tests required for vaccine or prevention trials. Other NIH initiatives, similar to CIPRA, need to be developed to focus on the needs in resource-poor countries.

SUPPORT OF ANIMAL FACILITIES

The National Center for Research Resources (NCRR), NIAID, and NCI have several programs in place that are designed to provide NHP for use in pathogenesis studies or in the evaluation of HIV/AIDS vaccine candidates, microbicides, and other physical or chemical barriers. New initiatives are in place to overcome the shortage of NHP, especially of Indian origin; however, expanded breeding programs and additional infrastructure are still needed to ensure adequate supplies of these animals. These expanded breeding programs will increase the number of SPF rhesus macaques available for AIDS-related research.

**INTRAMURAL AND
EXTRAMURAL
RESEARCH SITE
INFRASTRUCTURE**

NCRR also supports the Chimpanzee Biomedical Research Colonies for AIDS studies through the National Primate Research Centers (NPRCs). These NPRCs provide specialized facilities, scientific and technical personnel, breeding programs, and a wide variety of NHP species to support AIDS-related research. NCRR continues to sponsor an initiative to provide non-NPRC investigators with greater access to NPRC resources.

NIAID supports the development of the severe combined immunodeficiency (SCID) mouse model and the research for adaptation of transgenic animal models for HIV infection.

The National Heart, Lung, and Blood Institute (NHLBI) supports animal studies on transfusion-associated HIV infection and AIDS, on the development and evaluation of blood products, and on HIV-specific monoclonal antibody preparations for the prevention or treatment of HIV/AIDS.

To facilitate the advance of AIDS-related research, the NIH has provided funding for the improvement of biomedical research facilities and equipment domestically and on the NIH campus. The newly constructed NIAID Vaccine Research Center (VRC) specifically dedicated to the development of an HIV/AIDS vaccine is one of the latest facilities built by the NIH. This Center has the capability of performing research under good laboratory practices (GLP) and of producing small vaccines stocks under good manufacturing practices (GMP). In addition, the NIH is funding a new large facility to produce candidate HIV/AIDS vaccines lots to be used in HIV human vaccine clinical trials.

NCRR, through the General Clinical Research Centers (GCRCs) across the United States, provides the research infrastructure required for multidisciplinary studies on both children and adults. The Institutional Development Award (IDeA) Program, also administered by NCRR, is designed to help enhance the competitiveness for research funding of institutions in the United States with low success rates for grant applications to the NIH. This program should be expanded to include more scientists from minority-serving institutions, which traditionally have had low success rates for NIH grant applications.

Computers and high-speed computer networks are needed to support HIV protein configuration and structure, and also for better and faster communication among scientists at domestic and international sites. The National Library of Medicine (NLM) transition to a system of free Web-based access to MEDLINE and other NLM databases has enabled many investigators to obtain direct access. However, to obtain these benefits, AIDS and other biomedical researchers need to have the essential Internet infrastructure and training so that they can easily access relevant research information and also contribute new information to the ever-expanding

AIDS-related databases. This can still be a considerable challenge for researchers in remote, rural, or underserved communities. For researchers in major urban biomedical facilities, Internet access can also be problematic because of peak-hour congestion and the increasing size and complexity of the transmitted information. To overcome some of these problems, NLM is collaborating with the International Medical Informatics Association in South Africa to support those who develop and manage HIV/AIDS interventions, and the potential for information and communication technologies to accomplish these aims.

The NIH supports numerous repositories that provide resources for HIV/AIDS researchers. NHLBI maintains a repository of blood specimens from individuals with transfusion-associated HIV infection and from AIDS patients who have pulmonary disease. NCI sponsors the AIDS and Cancer Specimen Resource for well-documented tissue, biological samples, and associated clinical data collected from HIV-infected patients with cancer. NIMH, NIDA, and the National Institute of Neurological Disorders and Stroke sponsor the National NeuroAIDS Tissue Consortium. This specimen bank was established to standardize protocols to obtain central nervous system tissues from HIV-infected individuals to bolster research on HIV infection in the human brain. Through the AIDS Research and Reference Reagent Program, NIAID provides specific HIV reagents to investigators worldwide; however, the program needs to be continually expanded to include new reagents. Human specimen banks need to expand to store additional specimens. NHLBI and NIAID have established procedural guidelines to increase access to specimens from their patient cohorts and subjects in clinical trials by qualified investigators who are not collaborating in the specific studies supported by these Institutes.

SCIENTIFIC OBJECTIVES AND STRATEGIES

OBJECTIVE - A:

Provide training domestically and internationally in biomedical, social, and behavioral research on HIV, with an emphasis on multidisciplinary research in racially and culturally diverse settings domestically, and with attention to the needs of marginalized communities domestically and in developing countries with high incidence and/or high prevalence of HIV infection.

STRATEGIES:

- Increase predoctoral, doctoral, postdoctoral, and advanced research training across a broad range of AIDS-related disciplines.
- Support multidisciplinary training and mentoring programs to strengthen HIV/AIDS intervention research including behavioral interventions, vaccines, microbicides, therapeutics, sexually transmitted diseases in the context of HIV infection, interventions to interrupt mother-to-child transmission (MTCT), nutritional interventions, and substance abuse prevention and treatment.
- Expand the NIH AIDS LRP to bring minority U.S. scientists and physicians to the NIH in order to increase the cadre of trained HIV/AIDS researchers.
- Expand programs for HIV/AIDS research to develop culturally appropriate and relevant training and mentoring models to conduct research at U.S. minority-serving institutions.
- Develop and implement programs at domestic institutions, with attention to institutions serving minorities, to provide precollege training to attract students interested in behavioral and biomedical sciences related to HIV/AIDS research.
- Expand the number of domestic HIV/AIDS minority supplement awards to enhance the research capacity of minority individuals to make them more competitive for independent funding.
- Increase the number of funded U.S. minority investigators, for greater involvement and leadership in HIV research.
- Support HIV/AIDS research planning and organizational grants targeting domestic minority institutions and minority-serving communities. Emphasis should be placed upon grants that develop academy-community partnerships.
- Enhance opportunities through all ICs and programs to improve mechanisms for recruiting, training, mentoring, and retaining biomedical, behavioral, and social scientists in the conduct of interdisciplinary sex and gender analyses in HIV/AIDS research.

- Provide new opportunities and programs to attract newly trained investigators and established researchers from other fields to pursue HIV/AIDS research.
- Develop funding mechanisms to foster better linkages across AIDS-related scientific disciplines, including basic, clinical, epidemiologic, statistical, social, and behavioral science.
- Increase HIV/AIDS funding for the development of equal and productive partnerships between U.S. minority and majority institutions and community-based organizations (CBOs), with the funds located at the U.S. minority institution.
- Increase training to strengthen local capacity to conduct multidisciplinary AIDS-related prevention, vaccine, and therapeutic research in developing countries and emerging democracies by scientists from these countries.
- Strengthen cultural competency training and ethical training for the conduct of HIV/AIDS prevention, vaccine, and therapeutic clinical trials in domestic and international vulnerable populations.
- Provide support for all HIV/AIDS training materials such as CD- and Web-based training, and training sessions; all training materials must be adapted for local languages.
- Provide training in GLP/good clinical practices (GCP) for translational processes and in product development in both domestic and international settings conducting HIV/AIDS clinical trials or research.
- Implement new funding mechanisms to provide research training to nonphysician professionals (i.e., physician assistants and nurse practitioners) to increase the pool of HIV/AIDS minority researchers at domestic sites and at resource-poor settings.
- Support the training of biomedical and behavioral scientists in both developed and developing countries in the use of advanced computer and information technologies for HIV-related research, and ensure access to appropriate tools and equipment at the end of training.
- Support veterinary residency training programs in primate medicine at NPRCs or other primate facilities to help to increase the number of highly trained veterinarians who can manage the increasing needs for HIV/AIDS NHP-dedicated colonies.
- Support the training of veterinarian scientists who contribute to the growing need for interdisciplinary-trained researchers who help to understand both the microbial/infectious disease aspects as well as the animal model side of HIV/AIDS research in NHPs.

- Develop new models of integrated training that focus on the protection of human and animal subjects enrolled in HIV/AIDS clinical trials and on ethical issues of clinical trial design and implementation of vaccine and other prevention modalities in at-risk populations, in both domestic and international settings.
- Support training programs for personnel in resource-poor-setting institutions to strengthen the administrative and financial management capacity needed to conduct HIV/AIDS-related research.
- Expand programs to increase opportunities for scientists from developing countries and emerging democracies trained through the NIH to conduct AIDS research in their home countries (e.g., reentry grants).
- Develop new funding mechanisms and expand existing grant mechanisms, to link U.S. AIDS research scientists, industry partners, and relevant institutions with each other and with investigators and institutions in both developed and developing countries.
- Take advantage of existing AIDS clinical trial infrastructures to develop specific training programs in clinical trials methodology, including issues related to the design, recruitment, retention, target population dynamics, and analysis of data.
- Expand training programs on the effective use of HIV/AIDS antiretroviral drugs and prophylactic and therapeutic interventions for coinfections/opportunistic infections as well as adequate monitoring for patient safety.
- Develop training to prevent transmission of HIV and hepatitis C virus (HCV) in resource-poor health care facilities, including recruitment and retention of appropriate blood donors, predonation counseling of all blood donors, improvement of blood screening strategies and technologies, and appropriate use of transfusion.
- Support training opportunities for HIV prevention researchers interested in adding specific methodological skills to their research expertise (e.g., methods to conduct cost-effectiveness analyses, measurement of biologic outcomes in behavioral intervention studies, appropriate use of behavioral and social science measures in clinical trials, ethnographic and other qualitative methods, and network analysis).
- Support the training of members of HIV/AIDS-affected communities, to strengthen their ability to be informed partners in biomedical and behavioral science research.

OBJECTIVE - B:

Establish and maintain the appropriate infrastructure needed to conduct HIV research domestically and internationally with emphasis on populations of high prevalence.

STRATEGIES:

- Invest and expand funding in research infrastructure at U.S. minority-serving institutions to increase capacity to support HIV/AIDS research.
- Enhance, improve, and maintain research capacity and infrastructure in resource-poor settings with high HIV incidence, with particular emphasis on construction and operation of facilities for research on HIV prevention, including the development of vaccines and microbicides, as well as clinical trials for therapies and behavioral interventions.
- Enhance and improve the clinical trial research infrastructure for the conduct of prevention, vaccine, and therapeutics trials in domestic and foreign sites, including laboratory capacity, trained scientists and other personnel, appropriate participant cohorts, and mechanisms to address ethical issues such as the implementation of ethical committees and translated human rights documents.
- Enhance and improve research capacity and infrastructure to advance research on AIDS-associated coinfections (HCV, Kaposi's sarcoma-associated herpesvirus or human herpesvirus type 8, human papillomavirus, Epstein-Barr virus [EBV], TB, and malaria) and associated malignancies.
- Support an adequate infrastructure for producing HIV/AIDS vaccine candidates, for preventive and therapeutic vaccine trials, under GMP.
- Support adequate facilities and resources as well as appropriate ethical and procedural training to conduct HIV-related research in animal models.
- Expand the production of genetically defined SPF NHP, with emphasis on Indian-origin rhesus macaques.
- Develop and characterize appropriate reagents for use in HIV-related research conducted in different species of macaques and also other NHPs.
- Maintain programs that enhance the current research infrastructure, particularly the trans-NIH infrastructure, such as the Centers for AIDS Research (CFARs), the Research Facilities Improvement Program, and the GCRCs.
- Provide support for, and awareness of, the Biomedical Technology Resources Program for structural studies of HIV proteins and host proteins in the context of HIV infection.

- Provide for the long-term support of advanced in-country research in resource-poor settings participating in priority AIDS-related intervention research, such as methods to interrupt mother-to-child, sexual, or parenteral transmission, or trials of candidate HIV vaccines.
- Increase collaboration between CBOs and other Government-supported service providers (such as those funded through the Health Resources and Services Administration, U.S. Department of Veterans Affairs, and CDC) and academic researchers, to improve the quality and capacity of HIV/AIDS research endeavors in service settings.
- Establish and support quality-controlled repositories for, and ensure access by, qualified scientists to human samples (i.e., serum, peripheral blood mononuclear cell, plasma, patient-derived cell lines, cerebrospinal fluid, semen, breast milk, lymphoid tissues, and other key patient samples) and HIV strains from clinical trials and natural history and epidemiological studies, especially in complex study settings (e.g., MTCT studies).
- Develop, maintain, and effectively utilize domestic and international cohorts, repositories, and nested studies among populations experiencing emerging and ongoing HIV epidemics to establish databases that support analyses of host and viral characteristics.
- Maintain the present AIDS-related tumor registries, and ensure linkages between AIDS and cancer registries, for both domestic and international studies.
- Improve and adequately disseminate the process of requesting, prioritizing, and receiving HIV/AIDS laboratory samples, so that access is as timely and equitable as possible.
- Promote Internet connections and availability of pertinent information technology at health science centers, hospitals, outpatient clinics, CBOs, and other access points, both domestically and internationally, for HIV-related research and patient care.
- Develop statistical sampling methodologies, data collection protocols, and statistical analysis tools that are easy to use and adaptable to different settings; facilitate efficient statistical analysis and report generation and enhance standardization, when appropriate, in the context of HIV/AIDS research.
- Promote research in, and application of, medical informatics (e.g., high-performance computing) for HIV/AIDS research and clinical practice in resource-poor settings, both domestically and internationally.

- Enhance coordination and collaboration among NIH-supported investigators, other U.S. Government agencies, and other international agencies conducting HIV/AIDS research in the same developing countries.
- Develop efficient and effective systems for collecting and managing HIV/SIV(simian immunodeficiency virus)/SHIV(chimeric simian/human immunodeficiency virus) multiple-center and single-site clinical and animal model trial data; ensure timely and accurate dissemination of clinical and animal model trial information.

FY 2007 OAR
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Training, Infrastructure, and
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